Age-Change of Bone Mineral Density in the Distal Radius of Chimpanzees and Japanese Macaques

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Abstract Using peripheral quantitative computed tomography (pQCT), we evaluated and analyzed age-related changes in bone mineral density and other properties at the site of the distal radius in two catarrhines: chimpanzees and Japanese macaques. We found that the age changes in patterns are quite similar between the two species and the patterns are composed of three stages. Quantitative differences were found between the two species in the amount of bone mineral content and age of inflection points in the age-change diagrams. These differences appear to reflect differences in scaling effect and the life span between chimpanzees and Japanese macaques. Moreover, the age-change pattern of cortical bone density in chimpanzees and Japanese macaques closely resembled that in humans. This may reflect a similar pattern of bone turnover (metabolism of bone) throughout the life-cycle within catarrhines.

Keywords: age-change pattern, peripheral quantitative computed tomography (pQCT), life span, scaling effect, bone mineral density

Introduction

Recently, problems concerning bone properties such as osteoporosis, high risk of fracture, and decline of quality of life (QOL), have occurred with the advance of the ultra aging society. Investigators have performed physiological studies on some species of catarrhines, because macaques, baboons, and chimpanzees have some similarities to humans, including skeletal microstructures (Pope et al., 1989; Thompson et al., 1992; Schnitzler et al., 1993; Jerome et al., 1996), a clear adolescent period (Hamada, 1994; Hamada et al., 1998), regular menses (Johansson et al., 1968; Neil et al., 1969), and a spontaneous menopause (Pope et al., 1989). There have been, however, few basic studies with respect to age-changes of bone properties in catarrhines.

Analyzing bone geometric properties, Kimura described the age-related change of postcranial skeletons in adult Japanese macaques (Kimura, 1994). Champ and his co-workers described the effect of advancing age on bone mineral content in female

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rhesus monkeys (Champ et al., 1996). The flexion-points (inflection points at maturation in diagrams showing age change) of bone mineral content were obtained from DEXA scans at the following sites: total body, lumbar spine, and distal radius. They indicated that skeletal maturation in female rhesus monkeys occurred at the age of 11 years at the earliest. Since DEXA parameters are calculated for projective area, that is 2-D, not 3-D, it is very difficult to evaluate the internal structure of the bone and the actual geometrical variation resulting from bone turnover by DEXA.

There are several non-invasive methods to measure various properties of bone: Densitometer of radiographs, Dual Energy X-ray Absorptiometry (DEXA), peripheral Quantitative Computed Tomography (pQCT), and Ultra Sound Diagnosis (USD). Each of these has advantages and disadvantages, and we can select a method according to the purpose of the study. We choose pQCT for this study, because it has the advantage of providing three-dimensional bone mineral density (bone mineral content per cubic centimeter) and partial bone density and/or area for either cortical, or trabecular parts from the reconstructed cross-sectional density data. Using derived data the distribution of bone materials and structure is elucidated, and then, the bone mechanical strength and a clinical diagnosis of risk of fracture can be calculated. We report here the basic patterns of age-change of cross-sectional bone mineral density and other properties at the site of the distal radius in chimpanzees and Japanese macaques, and discuss the differences among patterns within catarrhines.

Materials and Methods

1. Chimpanzees (*Pan troglodytes*)

The chimpanzees used belong to Sanwa-Kagaku-Kenkyusho Co. Ltd. and the Primate Research Institute of Kyoto University in Japan. Some of them are kept in outdoor cages attached to a bedroom, some in a group breeding area inside a bedroom, and the others in individual cages. We measured chimpanzees at the annual health check in autumn. The total number of the data points with sexes and chronological ages are shown in Table 1a. Although some immature individuals were measured twice or three times, each point of these data (not averaged) was combined for the cross-sectional analysis (Table 1b). The pQCT scans were performed under anesthesia, using ketamine hydrochloride (Ketalar, Sankyo Co. Ltd.).

2. Japanese macaques (*Macaca fuscata*)

The Japanese macaques used belong to the Primate Research Institute of Kyoto University in Japan. They originate from the Takahama, Wakasa, or Arashiyama groups, and are all kept in open enclosures (L = 20 – 100 m, W = 20 – 30 m). Under anesthesia, using a 2:1 volumetric mixture of ketamine hydrochloride (Ketalar, Sankyo Co. Ltd.) and xylazine hydrochloride (Selactar, Bayer Co. Ltd.), in the dose of 0.15 cc/kg per body weight, pQCT scans were performed during the annual health check in autumn. Apart from these subjects reared in open enclosures, the subjects

Table 1. a: The total number of the date points with sexes and chronological ages in chimpanzee and Japanese macaque. The numbers in round brackets are the data points of the individuals measured more than once. b: Age and number of the immature individuals measured twice or three times in chimpanzee. c: measured twice, three times, or four times in Japanese Macaque.

a	Chimpanzee		Japanese Macaque	
Age (years)	Male	Female	Male	Female
0–1		1	2	1
2–3	1	3	4	4
4–5	1		5 (+ 9)	8 (+ 15)
6–7	0 (+ 1)	1 (+ 1)	5 (+ 2)	7 (+ 1)
8–9	0 (+ 6)	3 (+ 9)	1	4
10–11	2 (+ 1)		2	5
12–13	1 (+ 3)		4	3
14–15	1 (+ 1)	2	2	5
16–17		3	3	4
18–19		3	5	2
20–21		5	3	3
22–23		1	1	2
24–25	1			5
26–27	1	2		1
28–32	1	1		
Subtotal subjects 1	10	25	36	54
Total data points	22	35	47	70

b	Chimpanzee			
	Male		Female	
	Age (years)	numbers	Age (years)	numbers
	9, 10	1	7, 8	1
	13, 14	1	8, 9	4
	13, 13	1		
	8, 9, 9	1		
	7, 8, 8	1		
	Subtotal subjects 2	5		5
	data points	12		10

c	Japanese Macaque			
	Male		Female	
Age (years)	numbers	Age (years)	numbers	
	5, 5	2	5, 5	1
	5, 6	2	5, 6	1
	5, 5, 5	1	4, 5, 5, 5	3
	Subtotal subjects 2	5		5
	data points	11		16

kept in a group-cage (5 males and 5 females, aged 4–6 years) were measured longitudinally once a month, that total points of these data are 2–4 in each individual. Each point of these data (not averaged) was combined for the cross-sectional analysis (Table 1c). The total number of data points with sexes and chronological ages are listed in Table 1a (Matsubayashi et al., 1999).

3. pQCT (peripheral Quantitative Computed Tomography) analysis

In the present study, we diagrammatically examined age-change patterns of: 1) body weight (BW) and 2) periosteal area (PrA), 3) cortical bone Area (CtBA), 4) cortical bone mineral content (CtBMC), 5) cortical bone density (CtBD), 6) trabecular bone area (TbBA), 7) trabecular bone mineral content (TbBMC), and 8) trabecular bone density (TbBD) of cross-sectional radius.

In this study we used the pQCT apparatus, XCT Research SA and XCT 960A (Norland-Stratec Co. Ltd.). We mainly used the former apparatus, and it installs four collimators for different sizes of subjects and resolution. We used the largest collimator for both chimpanzees and Japanese macaques. A voxel size of 0.590 mm in Japanese macaques and 0.689 mm in Chimpanzees using XCT 960A, and a voxel size from 0.1 mm to 0.4 mm in both species using XCT Research SA, were used throughout the measurements. In XCT Research SA, 5, 10, and 15 mm/sec of CT speed were used throughout the measurement, and almost of the measurements were performed in the combination of 0.2 mm of voxel size and 5 mm/sec of CT speed, or 0.3 mm of voxel size and 10 mm/sec of CT speed.

Table 2. Coefficients of variation of scan data for ten measurements after repositioning using a female intact bone of Japanese macaques aged 15 years old.

PrA: Periosteal Area, CtBA: Cortical Bone Area, CtBMC: Cortical Bone Mineral Content, CtBD: Cortical Bone Density, TbBA: Trabecular Bone Area, TbBMC: Trabecular Bone Mineral Content, TbBD: Trabecular Bone Density.

VOXEL SIZE	CT SPEED	PrA	CtBA	CtBMC	CtBD	TbBA	TbBMC	TbBD
0.1	5	1.22	0.47	0.62	0.26	4.79	4.89	0.79
0.1	10	2.62	0.70	1.02	0.44	7.25	6.49	1.19
0.1	15	2.61	0.61	0.71	0.42	4.45	3.94	1.04
0.2	5	1.25	0.88	0.99	0.34	6.52	7.20	1.72
0.2	10	4.75	2.07	3.23	1.31	17.30	16.29	2.47
0.2	15	2.27	0.60	0.85	0.51	4.51	4.85	2.00
0.3	5	1.21	0.57	0.62	0.37	10.28	10.33	1.66
0.3	10	1.93	1.56	1.61	0.78	13.81	14.45	3.76
0.3	15	3.66	1.05	1.42	0.82	8.08	8.26	2.56
0.4	5	1.20	1.21	0.98	0.57	8.12	9.99	3.34
0.4	10	2.68	1.46	1.40	1.16	10.29	10.40	4.05
0.4	15	2.87	2.32	2.49	0.99	8.81	9.36	3.62

Table 3. Average for ten measurements after repositioning using a female intact bone of Japanese macaques aged 15 years old. Symbols are the same in Table 2.

VOXEL SIZE	CT SPEED	PrA	CtBA	CtBMC	CtBD	TbBA	TbBMC	TbBD
mm	mm/sec	mm ²	mm ²	mg/mm	mg/cm ³	mm ²	mg/mm	mg/cm ³
0.1	5	65.9	34.3	39.4	1149.1	4.3	1.8	418.1
0.1	10	63.8	34.5	39.8	1151.6	4.2	1.7	419.7
0.1	15	63.7	34.4	39.6	1151.4	4.3	1.8	423.4
0.2	5	68.5	34.7	38.1	1100.2	3.9	1.6	411.3
0.2	10	68.5	34.7	38.2	1099.7	4.0	1.6	409.9
0.2	15	67.3	34.7	38.3	1103.7	4.1	1.7	411.6
0.3	5	68.2	35.3	36.9	1045.9	3.9	1.6	408.8
0.3	10	66.3	35.7	37.7	1056.6	4.0	1.6	409.1
0.3	15	68.0	35.3	37.1	1049.7	3.9	1.6	414.8
0.4	5	66.3	35.8	36.1	1007.7	4.3	1.8	412.1
0.4	10	66.9	35.7	35.8	1004.5	4.4	1.8	414.4
0.4	15	66.6	35.6	35.7	1004.4	4.1	1.7	412.7

Since we performed measurements using various voxel sizes and CT speeds, we sensed a necessity to show the measuring errors and averages owing to the combination of the various metric parameters. Because of the problem of the anesthesia (we can't put the subjects under anesthesia for a long time), we could not measure living primates so many times. So, coefficients of variation (CV) and average were obtained from the same dried bone (a female intact bone of Japanese macaque aged 15 years old) for ten measurements after repositioning in the combination of 0.1, 0.2, 0.3, 0.4 mm of voxel size and 5, 10, 15 mm/sec of CT speed. CV and average of bone properties are listed in Table 2 and Table 3. In Table 2, scores in the set of 0.2 mm voxel size and 10 mm/sec of CT speed is highest. But we performed many measurements using this combination. Because, if we measure in smaller voxel size, we need to perform in slower CT speed to apply enough X-ray and get precise data; that is to say, it takes too much time to endure keeping anesthetized subjects. On the other hand, if we measure in larger voxel size, we don't need more time for faster CT speed but can't obtain very precise and detailed data. Although CV scores in the set of 0.2 mm voxel size and 10 mm/sec of CT speed in Table 2 are highest, CV scores among the individuals shown in Table 5 are higher than most of those in Table 2. So, we can ignore the measuring errors owing to the combination of the various metric parameters. In the table of averages, there is most difference (1004.4–1151.4 mg/cm³) among the scores of CtBD. However, performing most measurements in the combination of the 2 set of metric parameters and not so much but enough number of subjects considered, it is no problem to discuss the age-change of CtBD.

Before scanning, we measured the forearm length from radiale to stylium using

Table 4. Coefficients of variation of scan data for ten measurements of forearm length using same material (a female intact bone of Japanese macaque aged 15 years old). Symbols are the same in Table 2.

	PrA	CtBA	CtBMC	CtBD	TbBA	TbBMC	TbBD
CV	1.69	0.64	0.80	0.30	4.20	4.16	0.82

spreading caliper. After inserting the distal forearm of a subject into the gantry of pQCT, we fixed the wrist with a clamp and placed the fingers on a bridge. First, a scout (front-sectional) scan was performed only in distal portion. Based on the scout scan obtained, we determined the 4% position of the total forearm length from the styloid process of the radius (This portion is measured clinically because it is very good site for trabecular bone and it is one of the most suitable locations to examine metabolic effects on both cortical and trabecular parts). Then the main scan was performed to obtain bone density data. Each measurement took about 6 minutes.

If forearm length measured using spreading caliper is overestimated by 5 mm, 4% position of the total forearm length from the styloid process of the radius is more proximal to 0.2 mm. So, error of scan data owing to using spreading caliper must be shown. The above-mentioned measuring procedure was performed ten times to obtain coefficients of variation of scan data. Material is a female intact bone of Japanese macaque aged 15 years old and the scan were performed in the combination of 0.1 mm of voxel size and 5 mm/sec of CT speed. The result is listed in Table 4. The values are not different from those only performing reposition in Table 2 so much. So, the error using spreading caliper can be ignored.

Before analyzing the density parameters, we had to set the threshold separating soft tissue from cortical bone, and cortical from trabecular part. We used the 'half maximum height' algorithm to determine the threshold (Spoor et al., 1993; Ohman et al., 1997). This method verified fairly good applicability of the algorithm by an examination of the actual cross-section of the bone and the tomography of the cross-section of the bone (See the reference papers to know the details).

4. Statistical Analysis

We did not determine the significance of the differences between sexes and ages as the samples were too few and therefore, we discuss only the patterns of age-change. To draw age-change diagrams, we used the loess. smooth function (S-plus 4.0, Mathsoft Co. Ltd.) for smoothing. A regression window of 50% was used for all analyses. Although we could not display all of the raw data, as a summary of the raw data we also calculated the mean values, standard deviations and its coefficients of variation in immature and in the matured respectively. We regarded the chimpanzee subjects of 8–10 years of age and Japanese macaque subjects of 5–7 years of age as immature. We also regarded the chimpanzee subjects of 20 years of age or more and

Table 5. Mean values (mean), its standard deviations (sd) and coefficients of variation (CV) for various characters in immature and the matured. Age of immature: 8–10 years in chimpanzee and 5–7 years in Japanese macaque. Age of the matured: over 20 years in chimpanzee and over 15 years in Japanese macaque. Symbols are the same in Table 2.

Chimpanzee														
Male						Female								
Age group		Immature			The matured			Immature			The matured			
<i>n</i>		6			4			12			9			
character (unit)		mean	sd	CV	mean	sd	CV	mean	sd	CV	mean	sd	CV	
Age		9.1	0.5	5.5	26.5	4.2	15.8	9.0	0.5	5.6	23.9	3.7	15.5	
BW (kg)		47.0	5.2	11.1	57.9	10.1	17.4	36.4	4.7	12.9	44.0	6.2	14.1	
PrA (mm ²)		312.8	69.1	22.1	302.5	80.7	26.7	310.4	44.5	14.3	253.5	49.4	19.5	
CtBA (mm ²)		108.5	30.4	28.0	177.9	20.5	11.5	87.8	25.6	29.2	134.7	20.1	14.9	
CtBMC (mg/mm)		83.5	25.4	30.4	176.8	22.0	12.4	66.2	21.0	31.7	130.6	21.0	16.1	
CtBD (mg/cm ³)		763.2	28.8	3.8	992.9	43.7	4.4	747.5	32.2	4.3	969.4	58.9	6.1	
TbBA (mm ²)		142.7	51.6	36.2	52.0	5.9	11.3	155.7	44.5	28.6	54.8	34.7	63.3	
TbBMC (mg/mm)		64.5	25.1	38.9	22.5	3.2	14.2	69.9	20.1	28.8	24.1	15.6	64.7	
TbBD (mg/cm ³)		447.7	19.0	4.2	430.5	23.5	5.5	448.9	17.9	4.0	439.0	11.9	2.7	

Japanese macaque														
Male						Female								
Age group		Immature			The matured			Immature			The matured			
<i>n</i>		18			12			18			20			
character (unit)		mean	sd	CV	mean	sd	CV	mean	sd	CV	mean	sd	CV	
Age		5.7	0.5	8.8	18.5	1.8	9.7	5.7	0.5	8.8	20.4	3.8	18.6	
BW (kg)		10.4	1.9	18.3	13.5	2.6	19.3	7.4	0.9	12.2	9.4	2.4	25.5	
PrA (mm ²)		118.0	11.5	9.7	102.1	16.8	16.5	90.9	10.4	11.4	70.3	13.7	19.5	
CtBA (mm ²)		33.6	6.3	18.8	48.6	5.7	11.7	25.9	4.4	17.0	35.6	5.2	14.6	
CtBMC (mg/mm)		25.7	6.0	23.3	48.9	8.1	16.6	21.4	4.5	21.0	33.9	6.1	18.0	
CtBD (mg/cm ³)		760.4	44.7	5.9	1004.1	91.5	9.1	821.5	47.3	5.8	952.7	93.7	9.8	
TbBA (mm ²)		62.3	15.6	25.0	16.1	11.5	71.4	34.5	12.2	35.4	12.5	5.3	42.4	
TbBMC (mg/mm)		26.8	7.1	26.5	6.9	4.8	69.6	14.2	5.2	36.6	5.4	2.3	42.6	
TbBD (mg/cm ³)		428.9	12.2	2.8	429.2	10.5	2.4	410.5	15.7	3.8	431.3	12.1	2.8	

Japanese macaque subjects of 15 years of age or more as the matured (Hamada, 1994; Hamada et al., 1998 and 1999) (Table 5).

Results

1. Body Weight (BW) (Fig. 1): In chimpanzees, BW increased linearly until about 15 years of age, followed by slight increase or flat phase in both sexes. Sex difference became clear after approximately 8 years of age. The patterns of Japanese macaques were similar to those of chimpanzees for both sexes, that is, a linear increase phase until 7 or 8 years of age followed by an entirely flat phase.

2. Periosteal Area (PrA) (Fig. 2): In chimpanzees, PrA in males tended to increase up to 10 years of age and then decreased slightly, followed by a flat phase. In females, the age-change pattern was similar to that of males with PrA tending to increase until about 10 years of age and then showing a decreasing phase. Sex differences became clear after 20 years of age. PrA of male Japanese macaques increased rapidly up to about 5 years of age, then decreased slightly, and finally remained flat from the age of 10 years. PrA of females tended to trace a similar line to that in males but with a smaller area. Sex differences became significant after the age of 5 years.

3. Cortical Bone Area (CtBA) (Fig. 3): In chimpanzees, CtBA in males increased until about 16–17 years of age and then remained flat thereafter. In females, CtBA showed a similar pattern to that of males, that is, it increased until 12–13 years of age and increased slightly or remained flat thereafter. Age of the inflection points in male did not appear to coincide with that of female. Sex differences were apparent after 5 years of age and became significant after 15 years of age. The age-change pattern of CtBA in Japanese macaques was similar to that in chimpanzees, that is, it was composed of an increase and flat phases. Males grew linearly until about 10 years of age, followed by a flat phase. In females, the increase of CtBA seemed to cease at about 9–10 years of age and then the area remained flat. Sex differences became clear after 5 years of age.

4. Cortical Bone Mineral Content (CtBMC) (Fig. 4): The age-change pattern of CtBMC was very similar to that of CtBA for both chimpanzees and Japanese macaques. In chimpanzees, the inflection points on the graph were 16–17 and 13–14 years of age in male and female respectively. Clear sex differences were found after 15 years of age in chimpanzees. In Japanese macaques, the inflection points were 10 years of age in male and 9–10 years of age in female. Sex differences in became obvious after 8–10 years of age. Moreover, in both species, sex difference in age of the inflection points was regarded.

5. Cortical Bone Density (CtBD) (Fig. 5): In chimpanzees, CtBD remained flat until adolescence, increased rapidly up to 15–20 years of age, and remained flat or increased gradually thereafter. Clear sex difference seemed to be found at age in first inflection point; 10 years of age in male and 9–10 years of age in female. In

Figure 1. Relationship between age and body weight (BW) for chimpanzee and Japanese macaque. Average and (1 sd) for BW and age in adult are indicated by bars (solid line: males, broken line: females).

Figure 2. Relationship between age and periosteal area (PrA) for chimpanzee and Japanese macaque. Average and (1 sd) for PrA and age in adult are indicated by bars (solid line: males, broken line: females).

Figure 3. Relationship between age and cortical bone area (CtBA) for chimpanzee and Japanese macaque. Average and (1 sd) for CtBA and age in adult are indicated by bars (solid line: males, broken line: females).

Figure 4. Relationship between age and cortical bone mineral content (CtBMC) for chimpanzee and Japanese macaque. Average and (1 sd) for CtBMC and age in adult are indicated by bars (solid line: males, broken line: females).

Figure 5. Relationship between age and cortical bone density (CtBD) for chimpanzee and Japanese macaque. Average and (1 sd) for CtBD and age in adult are indicated by bars (solid line: males, broken line: females).

Figure 6. Relationship between age and trabecular bone area (TbBA) for chimpanzee and Japanese macaque. Average and (1 sd) for TbBA and age in adult are indicated by bars (solid line: males, broken line: females).

Figure 7. Relationship between age and trabecular bone mineral content (TbBMC) for chimpanzee and Japanese macaque. Average and (1 sd) for TbBMC and age in adult are indicated by bars (solid line: males, broken line: females).

Figure 8. Relationship between age and trabecular bone density (TbBD) for chimpanzee and Japanese macaque. Average and (1 sd) for TbBD and age in adult are indicated by bars (solid line: males, broken line: females).

Japanese macaques, the age-change patterns of density were very much similar to those of Chimpanzees. The first inflection point was about 5 years of age in male and 4–5 years of age in female respectively. Second was about 10 years of age in male and 8–9 years of age, and the mean densities of adults in macaques were also comparable to those of Chimpanzees. Sex difference was observed at age in inflection points.

6. Trabecular Bone Area (TbBA) (Fig. 6): The age-change patterns of TbBA were similar to those of PrA. The patterns were composed of an initial increase from birth to 10 years of age in chimpanzees and 5 years of age in male macaques, and then a slight decrease until 20 years of age in chimpanzees and until 10 years of age in male macaques. Perhaps because of the paucity of samples in the juvenile and infant age classes of macaques, TbBA in females did not show a juvenile and adolescent increase. The area decreased slowly until 5 years of age and then decreased rapidly until 10 years of age, followed by a flat phase. The variation among individuals was considerable (Table 5).

7. Trabecular Bone Mineral Content (TbBMC) (Fig. 7): The patterns of age-change were similar for the two species and also for those of TbBA of both sexes, that is, an increase followed by a decrease phase with the same age at peak. Ages at the peak were approximately 10 years in chimpanzees and 5 years in male Japanese macaques (the peak was not observed in macaque females).

8. Trabecular Bone Density (TbBD) (Fig. 8): In chimpanzees, the density did not change linearly or little decrease alternation with age, and it ranged consistently from 400 mg/cm³ to 480 mg/cm³. In both sexes, however, the TbBD appeared to decrease slightly from 10 years of age. In Japanese macaques the density also showed no significant changes with age. The density ranged from 400 mg/cm³ to 450 mg/cm³. TbBD showed no difference in variation among species or sexes. In both species and sexes, mean value in the matured remains about 425–450 mg/cm³ at diagrams (Table 5).

Discussion

The human species has a long life after menopause, that is, it has an elderliness phase in its life-cycle. During this period, bone suffers from aging processes such as osteoporosis. As a model for bone turnover (transferring from trabecular to cortical part), basic studies on non-human primates, especially, investigations of age-change in basic bone properties, are needed. However, there are few studies, which describe the age-change of non-human primates using such instruments as Dual Energy X-ray Absorptiometry (DEXA), Ultra Sound Diagnosis (USD), and peripheral Quantitative Computed Tomography (pQCT). There are a few exceptions, for example, Champ and his co-workers described the effect of advancing age on bone mineral content in female rhesus monkeys using DEXA (Champ et al., 1996). There are several studies on macaques describing epiphyseal union, another index of skeletal

maturation (Cheverud, 1981; Kimura, 1994; Kimura et al., 1995).

Ovariectomized female animals have been used for imitating the senescent (menopausal) animals (Jerome et al., 1994, 1997). For a comparison of natural aging processes, however, it is necessary to use naturally aging animals. In the present study, although based on cross-sectional data, we tried to evaluate age-change patterns of bone parameters in chimpanzees and Japanese macaques.

In previous study, age at the initiation of adolescent, when sex maturity is observed, was 8 and 7 years for males and females, respectively, in chimpanzees and 4.5 and 3.5 years for males and females, respectively, in Japanese macaques. Chimpanzees mature somatically around at 14 years of age, and macaques at 7 or 8 years of age (Hamada, 1994; Hamada et al., 1998, 1999). These ages were the used guidelines for the examination of skeletal maturation. However, in the present study, chimpanzees are thought to mature somatically around at 15–17 years of age, and macaques at 8–10 years of age. Moreover the diagrams of age-change for the seven parameters of bone properties indicated that a rapid change occurs at the vicinity of the beginning of adolescence. These data suggest an existence of tremendous activities in bone turnover concomitantly with sexual and somatic maturation. So, we think that the true maturation would be late a little more.

The decline in PrA after about 14 years in chimpanzees and 5 years in macaques in Fig. 2 is disturbing, since PrA are not thought to decrease in (unpathological) individuals with aging. This would strongly suggest nonrandom sampling (a cohort effect) or measurements of same individuals more than once, as a common problem in cross-sectional studies. There is no significant decline in BW in the older adults, which would not be consistent with the periosteal results. It's possible that in the distal 4% radius PrA might decrease after the age at the adults. Although the longitudinal study are necessary for revealing this problem, the other bone parameters are quite characteristic.

The patterns of age-change in chimpanzees are divided into three stages. At first stage until about 8–10 years of age, all of the bone parameters except for CtBD increase, and bone becomes increasingly larger internally and externally. Secondly, from 8–10 years of age to at least 15–17 years of age, bone becomes stiffer and stronger in the cortical region. Cortical bone parameters still increase, whereas trabecular bone parameters except for TbBD begin to decrease from 8–10 years of age and their diagrams of age-change have peak points. CtBD begins to increase linearly from 8–10 years of age to about 15–17 years of age. Finally, the diagrams of cortical part increase slightly or remain flat; on the other hand, trabecular parameters decrease gradually or remain stable. Thus, the bone turnover between the cortical and trabecular parts seems less active.

The age-change patterns of bone parameters in Japanese macaques are also divided into three stages as for chimpanzees. At first, that is, until about 4–5 years of age,

although TbBA and TbBMC decrease exceptionally in females, total bone size grows. Then, from 4–5 to 9–10 years of age, bone becomes stiffer and stronger in the cortical region because cortical bone increases both in CtBA and CtBMC, and CtBD begins to increase rapidly. On the other hand, parameters of trabecular bone except for TbBD decrease linearly in both males and females during this stage. Finally, bone seems to have little or no activity.

In the CtBA and CtBMC diagrams, we observed very similar patterns in the two species consisting of a linear increase phase followed by a flat or slight increase phase. Moreover it is very interesting to note that the diagrams of CtBD for both species resemble each other closely (Fig. 5). Density does not change until middle adolescence, and then it increases rapidly, and finally increases slowly or remains flat. The mean values of CtBD for the two species are also almost the same at immature ages (8–10 years of age in chimpanzees, 5–7 years of age in Japanese macaques) and the matured (Table 5). Comparing to the patterns of CtBA and CtBMC, the change pattern of CtBD is quite characteristic.

In the TbBA and TbBMC diagrams, except for age change patterns of macaque females, the patterns are similar between chimpanzees and macaques. The patterns consist of an initial increase phase until the middle of adolescence, a peak point, and a decreasing phase before the third stage. Although the pattern in female macaques, i.e., decreasing and flat, looks exceptional, this may have resulted from a bias of infants with extremely high TbBA and/or TbBMC values. Additional infant subjects need to be examined before concluding that female macaques are exceptional. The flat phase, starting at approximately 20 years of age in chimpanzees, seems to be continuous until 32 years at least. Although diagrams of TbBA and TbBMC resemble each other closely, the diagrams in TbBD do not show consistent increase or decrease patterns in the two species.

The patterns of age-change of CtBD (quality of bone) in both species look similar for the three stages. In adults, however, there are quantitative differences between the two species. For all bone parameters except density, the values for chimpanzees are 3 or 4 times those for Japanese macaques. The body weight of chimpanzees is also larger than that of macaques, with a close parallel to the bone parameters. This indicates that the parameters of bone quantities reflect body size actually. Moreover, the ages at the ends of each stage (the ages of the inflection points in the age-change diagrams) are different between the two species, being 8–10 and 15–17 years in chimpanzees, and 4–5 and 8–10 years in Japanese macaques. This difference may reflect the difference in life span.

The age-change patterns of bone properties studied earlier of humans (Lettgen, 1996), especially in CtBD, is similar to those of chimpanzees and Japanese macaques that have three stages. However, the density in humans is very low, perhaps because of differences in the threshold algorithm (500–600 mg/cm³). In humans, the inflec-

tion points in the diagrams of age-change were estimated to be 12–13 years of age and 20 years of age. These ages are slightly larger than those of Chimpanzees by approximately 1.2–1.3 times. If the life-span of humans is ca. 60 years, comparing the adolescent periods or the inflection points we could estimate that the life span of chimpanzees and macaques are approximately ca. 45–50 years and 25–30 years of age, respectively. The life span of chimpanzees is roughly twice as long as that of macaques.

We could not find a clear age-change demonstrating aging (senescence). This is due to the fact that the greatest ages of subjects, that we could sample, were 32 years for chimpanzees and 26 years for Japanese macaques. At these ages, females have not experienced menopause and are still active reproductively (although the outcome of reproduction is sometimes not successful in Japanese macaques of that age). As shown in the present study, female subjects of younger ages less than 10 years, although used frequently in many OVX (ovariectomized) experimental study models, seem to have many different physiological states including bone metabolism from true aged females as the bone properties have not attained maturation in the young adult stage. Therefore, young ovariectomized subjects are not suitable for aging model. It is important to continue the study of the relationship between age, reproductive physiology and bone properties using true aged individuals.

In the present study, the patterns of age-change in bone physical and physiological parameters are described for two catarrhine primates. We found many qualitative similarities in the age change patterns that demonstrate quantitative differences in the areas and the ages of the flexion points between sexes and the species, which are due to the differences in life-span and body size (scaling). But to describe detail of the aging process in bone properties, the addition of data from aged subjects and longitudinal study is indispensable.

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